

## SEQUENCE LISTING

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<120> METALLOPROTEASE ACTIVATION OF MYOSTATIN, AND METHODS OF MODULATING MYOSTATIN ACTIVITY

<130> JHU1800-3

<150> US 60/486,863

<151> 2003-07-10

<150> US 60/439,164

<151> 2003-01-09

<150> US 60/411,133

<151> 2002-09-16

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Thr	Ser	Ser	Arg	Leu	Glu	Ala	Ile	Lys	Ile	Gln	Ile	Leu	Ser	Lys	Leu	
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Val Gln Met Glu Gly Lys Pro Lys Cys Cys Phe Phe Lys Phe Ser Ser  
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Arg Gln Val Gln Lys Pro Thr Thr Val Phe Val Gln Ile Leu Arg Leu  
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Lys Thr Val Leu Gln Asn Trp Leu Lys Gln Pro Glu Ser Asn Leu Gly  
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Val Thr Asp Thr Pro Lys Arg Ser Arg Arg Asp Phe Gly Leu Asp Cys  
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 Gly Pro Val Gly Tyr Gly Asp Ile Thr Ala His Gln Gln Pro Ser Thr

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gcc Ala	acg Thr	gag Glu	gaa Glu	agc Ser	gag Glu	ctg Leu	tgt Cys	tcc Ser	aca Thr	tgt Cys	gag Glu	ttc Phe	aga Arg	caa Gln	cac His	144
35					40					45						
agc Ser	aag Lys	ctg Leu	atg Met	aga Arg	ctg Leu	cat His	gcc Ala	atc Ile	aag Lys	tcc Ser	caa Gln	att Ile	ctt Leu	agc Ser	aaa Lys	192
50					55					60						
ctc Leu	cga Arg	ctc Leu	aag Lys	cag Gln	gct Ala	cca Pro	aac Asn	atc Ile	agc Ser	cgg Arg	gac Asp	gtg Val	gtc Val	aag Lys	cag Gln	240
65					70					75					80	
ctg Leu	tta Leu	ccc Pro	aaa Lys	gca Ala	ccg Pro	cct Pro	ttg Leu	caa Gln	caa Gln	ctt Leu	ctg Leu	gat Asp	cag Gln	tac Tyr	gat Asp	288
85					90					95						
gtt Val	tta Leu	gga Gly	gat Asp	gac Asp	agt Ser	aag Lys	gat Asp	gga Gly	gct Ala	gtg Val	gaa Glu	gag Glu	gac Asp	gat Asp	gaa Glu	336
100					105					110						
cat His	gcc Ala	acc Thr	aca Thr	gag Glu	acc Thr	atc Ile	atg Met	acc Thr	atg Met	gcc Ala	aca Thr	gaa Glu	cct Pro	gac Asp	ccc Pro	384
115					120					125						
att Ile	gtt Val	caa Gln	gta Val	gat Asp	cgg Arg	aaa Lys	ccg Pro	aag Lys	tgt Cys	tgc Cys	ttt Phe	ttc Phe	tcc Ser	ttc Phe	agt Ser	432
130					135					140						
ccg Pro	aag Lys	atc Ile	caa Gln	gcg Ala	aac Asn	cgg Arg	atc Ile	gta Val	aga Arg	gcg Ala	cag Gln	ctc Leu	tgg Trp	gtt Val	cat His	480
145					150					155					160	
ctg Leu	aga Arg	ccg Pro	gcg Ala	gag Glu	gag Glu	gcg Ala	acc Thr	acc Thr	gtc Val	ttc Phe	tta Leu	cag Gln	ata Ile	tct Ser	cgg Arg	528
165					170					175						
ctg Leu	atg Met	ccc Pro	gtt Val	aag Lys	gac Asp	gga Gly	gga Gly	aga Arg	cac His	cga Arg	ata Ile	cga Arg	tcc Ser	ctg Leu	aaa Lys	576
180					185					190						
atc Ile	gac Asp	gtg Val	aac Asn	gca Ala	gga Gly	gtc Val	acg Thr	tct Ser	tgg Trp	cag Gln	agt Ser	ata Ile	gac Asp	gta Val	aag Lys	624
195					200					205						
cag Gln	gtg Val	ctc Leu	acg Thr	gtg Val	tgg Trp	tta Leu	aaa Lys	caa Gln	ccg Pro	gag Glu	acc Thr	aac Asn	cga Arg	ggc Gly	atc Ile	672
210					215					220						
gag Glu	att Ile	aac Asn	gca Ala	tat Tyr	gac Asp	gcg Ala	aag Lys	gga Gly	aac Asn	gac Asp	ttg Leu	gcc Ala	gtc Val	act Thr	tca Ser	720
225					230					235					240	
acc Thr	gag Glu	act Thr	ggg Gly	gag Glu	gat Asp	gga Gly	ctg Leu	ctc Leu	ccc Pro	ttt Phe	atg Met	gag Glu	gtg Val	aaa Lys	ata Ile	768
245					250					255						
tca Ser	gag Glu	ggc Gly	cca Pro	aaa Lys	cga Arg	atc Ile	cgg Arg	agg Arg	gac Asp	tcc Ser	gga Gly	ctg Leu	gac Asp	tgc Cys	gat Asp	816
260					265					270						

gag aat tcc tca gag tct cgc tgc tgc agg tac cct ctc act gtg gac 864  
 Glu Asn Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val Asp  
 275 280 285  
 ttc gag gac ttt ggc tgg gac tgg att att gct cca aaa cgc tat aag 912  
 Phe Glu Asp Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr Lys  
 290 295 300  
 gcg aat tac tgt tca gga gaa tgc gac tac atg tac ctg cag aag tat 960  
 Ala Asn Tyr Cys Ser Gly Glu Cys Asp Tyr Met Tyr Leu Gln Lys Tyr  
 305 310 315 320  
 ccc cac acc cat ctg gtg aac aag gcc agt ccg aga gga acg gct ggg 1008  
 Pro His Thr His Leu Val Asn Lys Ala Ser Pro Arg Gly Thr Ala Gly  
 325 330 335  
 ccc tgc tgc act ccc acc aag atg tct ccc atc aac atg ctt tac ttt 1056  
 Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr Phe  
 340 345 350  
 aac ggc aaa gag cag atc atc tac ggc aag atc cct tcg atg gta gta 1104  
 Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ser Met Val Val  
 355 360 365  
 gac cgc tgt ggc tgc tca tga 1125  
 Asp Arg Cys Gly Cys Ser  
 370

<210> 8  
 <211> 374  
 <212> PRT  
 <213> Danio rerio

<400> 8

Met His Phe Thr Gln Val Leu Ile Ser Leu Ser Val Leu Ile Ala Cys  
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Gly Pro Val Gly Tyr Gly Asp Ile Thr Ala His Gln Gln Pro Ser Thr  
20 25 30

Ala Thr Glu Glu Ser Glu Leu Cys Ser Thr Cys Glu Phe Arg Gln His  
35 40 45

Ser Lys Leu Met Arg Leu His Ala Ile Lys Ser Gln Ile Leu Ser Lys  
50 55 60

Leu Arg Leu Lys Gln Ala Pro Asn Ile Ser Arg Asp Val Val Lys Gln  
65 70 75 80

Leu Leu Pro Lys Ala Pro Pro Leu Gln Gln Leu Leu Asp Gln Tyr Asp  
85 90 95

Val Leu Gly Asp Asp Ser Lys Asp Gly Ala Val Glu Glu Asp Asp Glu  
 100 105 110

His Ala Thr Thr Glu Thr Ile Met Thr Met Ala Thr Glu Pro Asp Pro  
 115 120 125

Ile Val Gln Val Asp Arg Lys Pro Lys Cys Cys Phe Phe Ser Phe Ser  
 130 135 140

Pro Lys Ile Gln Ala Asn Arg Ile Val Arg Ala Gln Leu Trp Val His  
 145 150 155 160

Leu Arg Pro Ala Glu Glu Ala Thr Thr Val Phe Leu Gln Ile Ser Arg  
 165 170 175

Leu Met Pro Val Lys Asp Gly Gly Arg His Arg Ile Arg Ser Leu Lys  
 180 185 190

Ile Asp Val Asn Ala Gly Val Thr Ser Trp Gln Ser Ile Asp Val Lys  
 195 200 205

Gln Val Leu Thr Val Trp Leu Lys Gln Pro Glu Thr Asn Arg Gly Ile  
 210 215 220

Glu Ile Asn Ala Tyr Asp Ala Lys Gly Asn Asp Leu Ala Val Thr Ser  
 225 230 235 240

Thr Glu Thr Gly Glu Asp Gly Leu Leu Pro Phe Met Glu Val Lys Ile  
 245 250 255

Ser Glu Gly Pro Lys Arg Ile Arg Arg Asp Ser Gly Leu Asp Cys Asp  
 260 265 270

Glu Asn Ser Ser Glu Ser Arg Cys Cys Arg Tyr Pro Leu Thr Val Asp  
 275 280 285

Phe Glu Asp Phe Gly Trp Asp Trp Ile Ile Ala Pro Lys Arg Tyr Lys  
 290 295 300

Ala Asn Tyr Cys Ser Gly Glu Cys Asp Tyr Met Tyr Leu Gln Lys Tyr  
 305 310 315 320

Pro His Thr His Leu Val Asn Lys Ala Ser Pro Arg Gly Thr Ala Gly  
 325 330 335

Pro Cys Cys Thr Pro Thr Lys Met Ser Pro Ile Asn Met Leu Tyr Phe

340

345

350

Asn Gly Lys Glu Gln Ile Ile Tyr Gly Lys Ile Pro Ser Met Val Val  
 355 360 365

Asp Arg Cys Gly Cys Ser  
 370

<210> 9  
 <211> 50  
 <212> PRT  
 <213> Homo sapiens

<400> 9

Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu  
 1 5 10 15

Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp Gly Ser  
 20 25 30

Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met  
 35 40 45

Pro Thr  
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<210> 10  
 <211> 50  
 <212> PRT  
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<220>  
 <223> Mutant peptide portion of human myostatin

<400> 10

Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu  
 1 5 10 15

Leu Ile Asp Gln Tyr Asp Val Gln Gln Asp Asp Ser Ser Asp Gly Ser  
 20 25 30

Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met  
 35 40 45

Pro Thr  
 50

<210> 11



<211> 50  
 <212> PRT  
 <213> Artificial sequence

<220>  
 <223> Mutant peptide portion of human myostatin

<400> 11

Lys Asp Val Ile Arg Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu  
 1 5 10 15

Leu Ile Asp Gln Tyr Asp Val Gln Arg Ala Asp Ser Ser Asp Gly Ser  
 20 25 30

Leu Glu Asp Asp Asp Tyr His Ala Thr Thr Glu Thr Ile Ile Thr Met  
 35 40 45

Pro Thr  
 50

<210> 12  
 <211> 40  
 <212> PRT  
 <213> Homo sapiens

<400> 12

Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr  
 1 5 10 15

Asp Val Gln Arg Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp  
 20 25 30

Tyr His Ala Thr Thr Glu Thr Ile  
 35 40

<210> 13  
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 <212> PRT  
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<220>  
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<400> 13

Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr  
 1 5 10 15

Asp Val Gln Gln Asp Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp  
 20 25 30

Tyr His Ala Thr Thr Glu Thr Ile  
           35                          40

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<400> 14

Gln Leu Leu Pro Lys Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr  
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Asp Val Gln Arg Ala Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp  
                   20                          25                          30

Tyr His Ala Thr Thr Glu Thr Ile  
           35                          40

<210> 15  
 <211> 30  
 <212> PRT  
 <213> Homo sapiens

<400> 15

Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp  
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Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His Ala  
                   20                          25                          30

<210> 16  
 <211> 30  
 <212> PRT  
 <213> Artificial sequence

<220>  
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<400> 16

Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Gln Asp  
 1                  5                          10                          15

Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His Ala  
                   20                          25                          30

<210> 17

<211> 30  
 <212> PRT  
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<220>  
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<400> 17

Ala Pro Pro Leu Arg Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Ala  
 1 5 10 15

Asp Ser Ser Asp Gly Ser Leu Glu Asp Asp Asp Tyr His Ala  
 20 25 30

<210> 18  
 <211> 20  
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<400> 18

Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp Gly  
 1 5 10 15

Ser Leu Glu Asp  
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<210> 19  
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 <212> PRT  
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<220>  
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<400> 19

Glu Leu Ile Asp Gln Tyr Asp Val Gln Gln Asp Asp Ser Ser Asp Gly  
 1 5 10 15

Ser Leu Glu Asp  
 20

<210> 20  
 <211> 20  
 <212> PRT  
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<220>  
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<400> 20

Glu Leu Ile Asp Gln Tyr Asp Val Gln Arg Ala Asp Ser Ser Asp Gly

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Ser Leu Glu Asp  
20

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<210> 21
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<400> 21

Tyr Asp Val Gln Arg Asp Asp Ser Ser Asp  
1 5 10

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<211> 10
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<220>  
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<400> 22

Tyr Asp Val Gln Gln Asp Asp Ser Ser Asp  
1 5 10

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<220>  
<223> Mutant peptide portion of human myostatin

<400> 23

Tyr Asp Val Gln Arg Ala Asp Ser Ser Asp  
1 5 10